



NOTES

TYPE II HYPERSENSITIVITY REACTIONS

GENERALLY, WHAT ARE THEY?

PATHOLOGY & CAUSES

- Antibody-mediated hypersensitivity reactions; tissue-specific, broad spectrum of disease manifestations
- Disorder due to self-reactive B cells that produce **antibodies (e.g. IgM, IgG)** that **bind antigens on host cells**, form antigen-antibody complex at tissue site
 - Defective central tolerance → autoantibodies against self/intrinsic antigens
 - Embedded outside/extrinsic antigens into normal cell surface alter cell antigenicity

Common Type II hypersensitivity reactions

- Hemolytic disease of the newborn
- Autoimmune hemolytic anemia
- Immune thrombocytopenic purpura
- Bullous pemphigoid
- Pemphigus vulgaris
- Rheumatic fever
- Goodpasture syndrome
- Guillain-Barré syndrome
- Graves' disease
- Myasthenia gravis
- Pernicious anemia

TYPES

- Four pathologic mechanisms

Activation of complement system

- **IgM/IgG antibody binds fixed antigen** on cell → C1 binds Fc portion of IgM/IgG → classical pathway C2–C9 cleavage/activation → C3a–C5a anaphylatoxin production
 - Chemoattract promote degranulation of neutrophils, basophils, mast cells

(granules of lysosomal contents of leukocytes fuse, degrade target cell → cell death; mast cell degranulation contents include histamine → promote further immune cell response)

- Promote macrophage, monocytes **pro-inflammatory cytokine release**; interleukin (IL1), 6 (e.g. **Goodpasture's syndrome**, antibodies against Type IV collagen in lung, kidney)
- Membrane attack complex (MAC) formation (C5b–C9) → insertion into, disruption of cell membrane → impaired osmotic gradient → cell lysis (e.g. ABO mismatch in transfusion reaction, **hyperacute transplantation reaction**)

Opsonization, phagocytosis

- Antigen-opsonin C3b/IgG complex circulate
 - To spleen → fixed macrophages recognize IgG-bound antigens → phagocytosis
 - To liver → Kupffer cells recognize C3b-bound antigens → phagocytosis (**Autoimmune hemolytic anemia (AIHA)**, ABO, Rh-hemolytic disease of newborn)

Antibody-dependent cell-mediated cytotoxicity (ADCC)

- Natural killer cells bind Fc portion of **antibody-antigen complex** → release perforins, granzymes, granulysin → apoptotic cell death

Antibody-mediated cellular dysfunction (only non-cytotoxic mechanism)

- Physical **presence of antibody** at receptor binding site **impairs physiologic function**
 - **Activate**: thyroid hormone receptor in **Graves' disease**
 - **Inhibit**: acetylcholine receptor in **Myasthenia gravis (MG)**

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SIGNS & SYMPTOMS

- Acute hemolytic transfusion reactions
 - Fevers, chills; nausea/vomiting; flank, chest pain; dyspnea
- Autoimmune hemolytic anemia
 - Fatigue, jaundice, hepatosplenomegaly (HSM)
- Bullous pemphigoid
 - Abdominal, groin, extremity blistering
- Erythroblastosis fetalis
 - Kernicterus, death in fetus
- Goodpasture syndrome
 - Dyspnea, hemoptysis, hematuria
- Graves' disease
 - Tremor, insomnia, irritability, weight loss, tachycardia
- Guillain–Barre syndrome
 - Ascending paralysis
- Idiopathic thrombocytopenic purpura
 - Petechiae, skin ecchymoses
- Myasthenia gravis
 - Weakness, ptosis, diplopia, dysphagia
- Pemphigus vulgaris
 - Blistering of oral mucosa
- Pernicious anemia
 - Fatigue, glossitis, B₁₂ deficiency sequelae
- Rheumatic fever
 - Migratory polyarthritis, fever, +/- cardiac involvement

DIAGNOSIS

LAB RESULTS

- Coombs testing
 - **Direct:** detects **Fc region of bound antibodies** on red blood cells (RBCs) (e.g. ABO incompatibility)
 - **Indirect:** detects **circulating serum antibodies** against known antigen (e.g. anti-D)
- RBC antigen testing
- Immunohistochemistry (IHC)
- Diffuse radioactive iodine (RAI) uptake

OTHER DIAGNOSTICS

- Clinical presentation of disease-specific symptoms

TREATMENT

MEDICATIONS

- Corticosteroids
- Severe reactions may require plasmapheresis/immunosuppressants

TYPE II HYPERSENSITIVITY EXAMPLES

SYNDROME	SIGNS & SYMPTOMS	ANTIBODY TARGET	PATHO- PHYSIOLOGY	DIAGNOSTIC TESTING
ACUTE HEMOLYTIC TRANSFUSION REACTIONS	Fevers, chills; nausea/vomiting; flank, chest pain; dyspnea	A/B antigen types on red blood cells (RBC)	Complement mediated	Clinical; prevent with proper RBC antigen type screening
AUTOIMMUNE HEMOLYTIC ANEMIA	Fatigue, jaundice, hepatosplenomegaly (HSM)	RBC cell membrane	Opsonization	Coombs testing
BULLOUS PEMPHIGOID	Abdominal, groin, extremity blistering	Hemidesmosome (BP180)	ADCC, Ab-mediated cellular dysfunction	Clinical; immunohistochemistry (IHC): linear IgG pattern along skin basement membrane
ERYTHROBLASTOSIS FETALIS	Fetal: kernicterus, death Maternal: none	Fetal RBC antigens	Complement mediated	Abdominal, groin, extremity blistering
GOODPASTURE SYNDROME	Dyspnea, hemoptysis, hematuria	Renal, lung Type IV collagen	ADCC	IHC: linear Ab pattern at kidney, lung
GRAVES' DISEASE	Tremor, insomnia, irritability, weight loss, tachycardia	Thyrotropin (TSH) receptor	Ab-mediated cellular dysfunction	TSH, T4 levels, diffuse radioactive iodine (RAI) uptake
GUILLAIN-BARRE SYNDROME	Ascending paralysis	Motor neurons	ADCC	Clinical; cerebrospinal fluid (CSF) elevated protein
IDIOPATHIC THROMBOCYTOPENIC PURPURA	Petechiae, skin ecchymoses	Platelets	Opsonization	Platelets < 20 k, normal coagulation study
MYASTHENIA GRAVIS	Weakness, ptosis, diplopia, dysphagia	Nicotinic acetylcholine receptors	Ab-mediated cellular dysfunction	Acetylcholine Ab testing
PEMPHIGUS VULGARIS	Blistering of oral mucosa, may generalize	Desmoglein	ADCC, Ab-mediated cellular dysfunction	Clinical; IHC: "fish net" IgG pattern
PERNICIOUS ANEMIA	Fatigue, glossitis, B12 deficiency sequelae	Parietal cells	ADCC	Clinical; anemia, B12 lab testing
RHEUMATIC FEVER	Migratory polyarthritis, fever, +/- cardiac involvement	Fc of IgG (by IgM Ab; AKA rheumatoid factor)	ADCC	Clinical criteria

Ab: antibody, ADCC: antibody-dependent cellular-mediated cytotoxicity, HSM: hepatosplenomegaly, IHC: immunohistochemistry, RAI: radioiodine uptake